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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,135	02/13/2002	Akemichi Baba	010541A	5435

23850 7590 09/08/2004

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,135	BABA ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/14/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/835627.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending in the application.

This Office Action is in response to the Amendment filed on 6/14/04.

Response to Amendment

Acknowledgement is made of Applicant's submission of sequence listing in paper copy and CRF. The objection is withdrawn.

The rejection of claims 1-8 under 35 U.S.C.101 has been withdrawn in light of Applicant's amendment of the claims.

Claims 1-8 and newly added claims 9-18 stand rejected under 35 U.S.C. 112 1st paragraph for reasons set forth of the record mailed on 2/13/04 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and newly added claims 9-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 18 is drawn to a non-human mammalian model animal deficient of PACAP, wherein said animal is used for studying the *in vivo* function of PACAP-dependent signaling in

pathological disorders. This claim provides another utility for the claimed non-human mammal besides being a psychiatric model as recited in claim 1. However, the specification does not provide any teaching with regard to what type of pathological disorders PACAP-dependent signaling is associated with. As such, this utility lacks real world use because it appears to be an invitation for further research of the *in vivo* function of the PACAP, which Applicants do not known at the time of filing. Therefore, the claimed non-human mammalian model animal is not enabled for this embodiment.

In response to this rejection, Applicants argue that the specification teaches technologies (other than ES cell technology) such as RNAi or random integration for making the claimed transgenic non-human animal. Applicants argue that such technologies are enables one skilled in the art to select an appropriate technology to obtain the claimed model mammalian animal. Applicants further argue that the heterozygous transgenic mouse showed a reduction in expression of the mature peptide while homozygous mice showed a complete disappearance of expression, and the data presented in the specification (page 23, lines 7-9, and table 1) teaches that the heterozygous mouse can be used as a psychiatric model. Furthermore, Applicants argue that a transgenic animal having PACAP partial deficiency is obtainable and provides results that can be used as psychiatric model. Applicants further cite Matsuyama et al. to demonstrate the successful application of PACAP deficiency to heterozygous animals. Moreover, Applicants argue that the PACAP gene deficient animals are useful for studying the *in vivo* function of PACAP-dependent signaling, and the link between PACAP deficiency and psychiatric behavior is taught by the specification, thus a person skilled in the art would be able to practice the presently claimed invention with regard to a variety of symptoms. Lastly, Applicants submit

several references to demonstrate that PACAP deficiencies was conventionally related to psychiatric disorders. Applicants thus conclude that the invention is enabled by the instant specification.

The above arguments have been fully considered but deemed unpersuasive. The reasons for the non-enablement of the claimed invention was discussed in detail in the Office Action mailed on 2/13/04. In response to Applicants' argument with regard to technologies of making the claimed transgenic non-human animal, contrary to Applicants' assertion, the specification does not teach a method of making said transgenic non-human animal by methods such as random integration or RNAi, wherein the PACAP gene is specifically disrupted. As discussed in the previous office action, whether random integration would result in a transgenic non-human animal with targeted disruption of the endogenous PACAP gene is unpredictable. In addition, neither the specification nor prior art teach a method of making a transgenic non-human animal using inhibitory RNA molecule. As such, the specification fails to enable one of skilled in the art to make the claimed non-transgenic mammal.

In response to Applicants' argument with regard to heterozygous transgenic animals, it is considered not persuasive because reduction in the expression of endogenous PACAP is not considered as a phenotype that can be used as psychiatric model. In fact, the specification discloses that the heterozygous PACAP knockout mouse has no behavioral difference between in the open field test with the wild type mouse (see page 23, lines 7-9). It appears that Applicants misconstrue the reasons for the non-enablement of the heterozygous transgenic animal in the previous office action. The Examiner has never stated that a transgenic animal with partial deletion of the PACAP gene cannot be made, rather the unpredictability lies in whether the

heterozygous animal would have the same phenotype as the homozygous transgenic animal. The phenotype of the transgenic animal is essential for the enablement of the claims because one would not know how to use a transgenic animal without any phenotype as a psychiatric model as claimed. Matsuyama et al. teach that the PACAP heterozygous transgenic knockout mouse display impaired long-term potentiation (LTP) *in vivo*. However, this phenotype does not support the enablement of such mice as a model for psychiatric disorder as claimed. Neither the specification nor the prior art teaches an association between a psychiatric disorder and the disruption of the PACAP. Therefore, the instant specification fails to provide the enablement of the claimed transgenic non-human mammal.

In response to Applicants' argument of using the claimed transgenic non-human animal for psychiatric behavior, Applicants are again reminded that the phenotype of the claimed transgenic non-human mammal is the critical element for the use of said mammal. The only disclosed use for the claimed non-human animal is a psychiatric model. The specification discloses that this model can be used to screening drugs that treats human psychiatric disorder. The specification only discloses a homozygous PACAP knockout mouse having the phenotype of hyperactivity which is reversible by haloperidol, increased exploratory activity and reduced anxiety. It is unclear whether human with the same disclosed phenotype is result from the disruption of the PACAP gene. In addition, contrary to Applicants' assertion, neither the specification nor prior art teach an association between a psychiatric disorder and PACAP disruption in human. The art only teaches the association PACAP disruption and LTP in a mouse model (Matsuyama et al., Gyula et al. and Otto et al), which does not predict the same relationship in human psychiatric disorder. Hishmoto et al. teach that PACAP mouse display

deficit in LTP and exhibits phenotype including hyperlocomotion and explosive jumping. However, the reference also fails to teach whether such phenotype is predictive of same behavior in human. Zan et al. teach a method of producing knockout rats by ENU mutagenesis. This reference does not teach any correlation between PAPCAP deficiencies and psychiatric disorder. As such, these references fail to support the claimed non-human mammal as a psychiatric model for human. Moreover, the phenotype of a transgenic animal is unpredictable. One cannot predict the same phenotype in another transgenic animal based on the phenotype of a mouse model (see previous office action for detailed discussion). As such, the disclosure of the instant specification does not support the enablement for any transgenic non-human mammal as a psychiatric model. Since the only disclosed use of the non-human mammal is a model for human psychiatric disorder which is not enabled for reasons given above, one skilled in the art would not know how to use the claimed invention. Therefore, for reasons set forth of the record mailed on 2/13/04 and above, this rejection is maintained. Newly added claims 9-18 are rejected for same reasons as discussed above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine Qian, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER